PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61B 17/36

A1

(11) International Publication Number: WO 99/56641

(43) International Publication Date: 11 November 1999 (11.11.99)

(21) International Application Number: PCT/GB99/01354

(22) International Filing Date: 30 April 1999 (30.04.99)

(30) Priority Data:
9809342.0 30 April 1998 (30.04.98) GB

(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

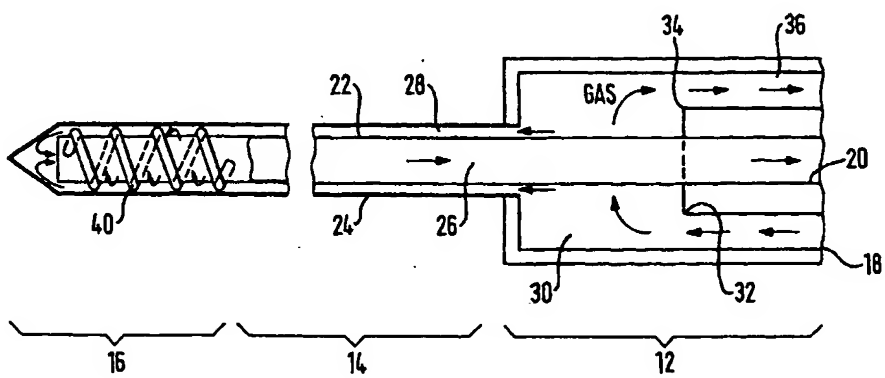
Published
With international search report.

(71) Applicant *(for all designated States except US)*: SPEMBLY MEDICAL LIMITED [GB/GB]; Newbury Road, Andover, Hampshire SP10 4DR (GB).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: CUFF, Louise [GB/GB]; 65 Armstrong Rise, Charlton, Andover, Hampshire SP10 4EB (GB).

(74) Agent: HOLMES, Miles, Keeton; D Young & Co., 21 New Fetter Lane, London EC4A 1DA (GB).

(54) Title: CRYOSURGICAL APPARATUS



(57) Abstract

Cryosurgical apparatus, for example, a probe (10) is described which produces cooling by vaporization of a liquid cryogen, such as a liquid nitrogen. Means (40) are located adjacent to the cooling region of the probe to define a tortuous flow path for the cryogen to, through, or from, the cooling region, in order to improve the thermal efficiency of the probe. In one form, the means (40) consists of a wire wound into a spring shape to define a helical path between concentric conduits (22, 24) defining inlet and exhaust passages (26 and 28) for the cryogenic fluid.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania
AM	Armenia
AT	Austria
AU	Australia
AZ	Azerbaijan
BA	Bosnia and Herzegovina
BB	Barbados
BE	Belgium
BF	Burkina Faso
BG	Bulgaria
BJ	Benin
BR	Brazil
BY	Belarus
CA	Canada
CF	Central African Republic
CG	Congo
CH	Switzerland
CI	Côte d'Ivoire
CM	Cameroon
CN	China
CU	Cuba
CZ	Czech Republic
DE	Germany
DK	Denmark
EE	Estonia
ES	Spain
FI	Finland
FR	France
GA	Gabon
GB	United Kingdom
GE	Georgia
GH	Ghana
GN	Guinea
GR	Greece
HU	Hungary
IE	Ireland
IL	Israel
IS	Iceland
IT	Italy
JP	Japan
KE	Kenya
KG	Kyrgyzstan
KP	Democratic People's Republic of Korea
KR	Republic of Korea
KZ	Kazakstan
LC	Saint Lucia
LI	Liechtenstein
LK	Sri Lanka
LR	Liberia
LS	Lesotho
LT	Lithuania
LU	Luxembourg
LV	Latvia
MC	Monaco
MD	Republic of Moldova
MG	Madagascar
MK	The former Yugoslav Republic of Macedonia
ML	Mali
MN	Mongolia
MR	Mauritania
MW	Malawi
MX	Mexico
NE	Niger
NL	Netherlands
NO	Norway
NZ	New Zealand
PL	Poland
PT	Portugal
RO	Romania
RU	Russian Federation
SD	Sudan
SE	Sweden
SG	Singapore
SI	Slovenia
SK	Slovakia
SN	Senegal
SZ	Swaziland
TD	Chad
TG	Togo
TJ	Tajikistan
TM	Turkmenistan
TR	Turkey
TT	Trinidad and Tobago
UA	Ukraine
UG	Uganda
US	United States of America
UZ	Uzbekistan
VN	Viet Nam
YU	Yugoslavia
ZW	Zimbabwe

CRYOSURGICAL APPARATUS

This invention relates to cryosurgical apparatus for producing cryogenic cooling by vaporization of a liquid cryogen, such as liquid nitrogen. The invention is particularly suitable for probe apparatus including a cooled tip region, but the invention is not limited exclusively to such apparatus.

Many different designs of cryosurgical probe have been proposed to generate cooling at a boiling region at, or adjacent to, a tip of the probe. For example, reference is made to GB-A-2289412, GB-A-2289413, GB-A-2289414, and GB-A-2289510, which illustrate a probe employing a so-called heatsink device arranged adjacent to the boiling region, and in intimate contact with the tip casing. The heatsink device consists of a lobed insert defining parallel axial exhaust paths through which the cryogen is channeled as it leaves the boiling region, to improve the thermal efficiency of the probe.

In contrast to prior designs, one aspect of the present invention is to guide the cryogen along a tortuous cryogen flow path at or adjacent to the cooling region.

The term "tortuous" is used herein in a very broad sense to mean that the flow path is generally longer than the linear (and/or longitudinal) dimension of the means defining the tortuous path. With such a tortuous path, the cryogen flow will not be purely in a single linear direction as the cryogen flows through the means defining the tortuous path.

The use of such a tortuous flow path can improve the thermal efficiency of the apparatus by increasing the path length through the cooling region, and thus increase the length of time that the cryogen spends at, or adjacent to, the cooling region. Furthermore, the contact area with the cryogen will generally be greater than an alternative arrangement employing a non-tortuous path, to promote greater thermal coupling between the cryogen and the surrounding walls defining the flow path.

The tortuous path may be at the boiling region itself, or it may be immediately upstream and/or immediately downstream of the boiling region, forming a part of the feed into, or the exhaust from, the boiling region.

Preferably, the tortuous path is predetermined or is predeterminable. In other words, the tortuous path is well defined, rather than being a random path through a porous medium. This can provide better control of the fluid flow, and predictable cooling behavior.

A single tortuous path may be provided, or a plurality of tortuous paths may be provided along side, or "in parallel" with, each other. In the latter case, it is preferred that the number of such paths "in parallel" with each other is less than about 20, more preferably less than about 15, more preferably less than 10, more preferably less than 5, more preferably less than 4, and more preferably less than 3.

The effect of a tortuous flow path is to concentrate, at least to some extent, the cooling cryogenic effect in the region of the means defining the tortuous path. This effect can be used to control, in a unique manner:

(a) the position on the probe at which the iceball will grow, in use; and

(b) the shape of the iceball (for example, if a non-spherical iceball is desired).

Preferably, the tortuous path is in intimate contact with an external wall portion of the cooling region of the apparatus. This can provide optimum thermal coupling between the cryogen flow path and the external cooling surface of the apparatus.

Preferably, the tortuous path is defined by one or more surfaces or walls of heat conductive material.

The tortuous path may be defined by one or more labyrinth walls, or by one or more baffles. However, in a particularly preferred embodiment, the tortuous path is defining by a helical wall. **In one form**, the helical wall may comprise a strip, or wire, which is wound around an inner carrier. The inner carrier preferably is one of a plurality of concentric conduits for feeding cryogen to, and exhausting cryogen from, the boiling region, the helical strip or wire being received between the two conduits for defining a helical path in the outer of the concentric flow paths. In an alternative form, the helical wall may be defined by a helical fin fitted to, or integrally formed with, one of the inner and outer conduits.

In a closely related aspect, the invention provides a cryosurgical probe comprising a probe tip, a boiling region at or adjacent to the probe tip for generating cooling by

vaporization of liquid cryogen supplied through the tip, and means located at or adjacent to the tip for defining a non-axial flow path, the flow path having a path length greater than the axial length of said means. The term "non-axial" is used herein broadly to mean that the flow path past or through said means includes at least one component in a direction other than the axial direction (i.e. the flow path direction is not purely axial).

In a further closely related aspect, the invention provides cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of liquid cryogen, and means located at or adjacent to the cooling region and defining a substantially helical cryogen flow path.

In a further aspect, the invention provides cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of liquid cryogen, and means located at or adjacent to the cooling region and defining a tortuous flow path for cryogenic fluid, such that, in use, the apparatus creates a non-spherical iceball shape. Preferably, the iceball is elongate and/or at least partly concave.

In a further aspect, the invention provides cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of liquid cryogen, and means located at or adjacent to the cooling region and defining a tortuous flow path for cryogenic fluid, such that, in use, the position of the iceball is defined by the position in the apparatus of said means defining the tortuous flow path.

In a further aspect, the invention provides cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of liquid cryogen, and means located at or adjacent to the cooling region and defining a tortuous flow path, the amount of tortuosity varying and being dependent on the position in the cooling region. In one form, the tortuosity varies (abruptly) from a maximum at one position to a minimum (zero) at a second position.

Embodiments of the invention are now described, by way of example only, with reference to the accompanying drawings, in which:

Fig. 1 is a schematic cross-section through a first embodiment cryosurgical probe;

Fig. 2 is a schematic view illustrating the construction of the helical path at the tip;

Fig. 3 is a schematic view illustrating an alternative construction of helical path;

Fig. 4 is a schematic view illustrating a further alternative construction of helical path;

Fig. 5 is a schematic cross-section through the tip of a second embodiment of probe;

Figs. 6a-6d illustrate how the position of the iceball can be controlled according to the design of the probe;

Figs. 7a-7d illustrate how the shape of iceball can be controlled according to the design of the probe;

Fig. 8 illustrates an alternative member for defining a helical flow path; and

Fig. 9 is a schematic view illustrating an alternative tortuous flow path.

Referring to Figs. 1 and 2, a cryosurgical probe 10 comprises a handle portion 12, a stem portion 14, and a tip portion 16. In the present embodiment, liquid cryogen, for example, liquid nitrogen, is supplied to the probe handle 12 through an inlet port 18, and exhaust cryogen leaves the probe handle 12 through an exhaust port 20.

The stem includes first and second concentric conduits 22 and 24 defining an inner passage 26 and an outer passage 28 extending between the handle 12 and the probe tip 16. In the present embodiment, the outer passage 28 provides a cryogen inlet path for delivery of cryogen liquid to the probe tip; the inner passage 26 provides an exhaust passage for removal of exhaust cryogenic fluid from the tip region 16.

The inner conduit 22 extends from the probe tip 16 to the exhaust port 20 to provide a direct path for exhaust cryogenic fluid. The outer conduit 24 extends from the probe tip 16 into the handle 14 to a first outlet of a transfer chamber 30. The transfer chamber has an inlet 32 coupled to the cryogen inlet port 18, and a second outlet 34 coupled to a bypass exhaust port 36. The purpose of the transfer chamber 30, and of the bypass path, is similar to that described in the above-mentioned GB patent publications. As the probe 10 initially cools when liquid nitrogen is first introduced into the probe at the start of a procedure, there will be a substantial amount of evaporation of the cryogenic liquid in the inlet passages. This results in a large amount of exhaust gas being generated upstream of the tip, at least until the probe has cooled to near cryogenic temperatures.

(Once the low temperatures have been reached, then the amount of evaporation upstream of the tip will be reduced to normal levels.) During the initial cooling stage, the transfer chamber serves to enable the gas in the inlet passages to vent away through the bypass port 36. This improves the flow of liquid reaching the tip 16, and allows rapid "cool down" of the probe tip.

In the present embodiment, the difference in the diameters of the confronting surfaces of the inner and outer conduits 22 and 24 is typically of the order of 1 mm or less. For example, the total diametric spacing may be about 0.5 mm. This means that the cross-sectional area of the inlet passage 28 in the stem 14 is relatively small. It will be appreciated that the flow of liquid into such a narrow region could be severely disrupted by the presence of gas if the bypass port 36 were not provided. However, the provision of the bypass port 36, and the design of the transfer chamber 30 promote separation and venting of the gas from the main flow of cryogenic liquid.

At a position adjacent to the tip 16, a helical guide 40 is located between the inner and outer conduits 22 and 24, to define a helical entry path into the tip region. Such a helical path is an example of a tortuous path which functions to increase the thermal efficiency of the probe for the following reasons:

(a) the cryogenic liquid spends a greater amount of time in the tip region, thus providing longer for the cryogenic liquid to boil and to transfer its cooling energy to the tip;

(b) the guide 40 provides additional surface area for heat transfer at the tip region, to allow better thermal coupling between the tip and the cryogenic fluid;

(c) the tortuous path introduces swirling, or turbulent flow, thereby increasing thermal contact between the liquid and the surrounding tip.

Referring to Fig. 2, in the present embodiment, the guide 40 is formed from metal wire, for example, stainless steel wire or aluminum wire, wound into a spring shape 42. The spring shape 42 is mounted over the end of the inner conduit 22, and can be secured in position by any suitable means, for example, by welding.

The wire is dimensioned so that the guide 40 will be in intimate contact with both the inner conduit 22 and the outer conduit 24 when the probe is assembled. The wire may

also provide accommodation of tolerance variations by being able to be squeezed, to some extent, between the inner and outer conduits. Such a construction of the guide 40 is extremely simple and cheap, and can be fitted to existing probe designs without requiring major re-designing of the probes.

In tests, the effect of the guide 40 has been observed. It has been found that the guide does improve (reduce) the cool down time of the probe noticeably. Also, in contrast to many existing probes, virtually no liquid was returned in the exhaust path. This indicates that the guide 40 provides extremely good thermal coupling between the cryogenic liquid, and the tip material.

The effect of the guide 40 was also observed by changing the position and length of the guide along the stem 14. It has been found that the guide 40 effectively concentrates the cooling region of the probe. This can enable the cooling region to be engineered more precisely to suit particular applications.

For example, Figs. 6a-6d illustrate how, in use, the position of the frozen iceball 60 can be controlled by the position in the probe of the helical guide (shown schematically at 40). If the helical guide 40 is moved away from the tip, the iceball is centered about a position which also moves back from the tip (Figs. 6b and 6c). Similarly, if the helical guide 40 is moved towards the tip, the iceball center moves correspondingly forward (fig. 6d).

The iceball position shown in Fig. 6c is especially significant and useful, because the frozen region extends exactly up to, but not beyond, the tip of the probe. This means that the probe tip can be used to precisely position the probe by advancing it to bear against, for example, a known organ, or known internal tissue, without freezing that tissue.

Figs. 7a-7d illustrate how the shape of the frozen iceball 60 can be controlled by the length and configuration of the helical guide 40. For example, Figs. 7a and 7b illustrate the variation in iceball length for different lengths of helical guide 40.

Fig. 7c illustrates how a waisted iceball region 60 can be created by using first and second helical guides 40 and 40 spaced apart to define two "focii" of freezing. The amount of cooling generated in the region 62 between the helical guides 40 is smaller

than the amount of cooling at each guide 40, and this leads to a waisted shape, or at least a shape which includes a generally non-convex region. The shape has an axis of rotational symmetry, corresponding to the probe axis.

Figs. 7d illustrates an alternative helical guide arrangement for producing a waisted frozen iceball 60. In this arrangement, a single helical guide 40 is employed, but having a varying pitch. The pitch is closely spaced at the end regions 64 of the guide to focus the cooling in those regions, and relatively wide spaced at the central region 66, providing relatively less cooling in the central region.

It will be appreciated that the invention can therefore provide the probe designer with great flexibility and versatility for a given design of probe. Different iceball positions, sizes and shapes can be generated from the same basic probe design simply by fitting tortuous guides (for example helical guides) at one or more desired positions within the probe. This can provide for very economical manufacture of a wide variety of probes, and also enable probes to be produced for custom requirements very quickly and easily.

Figure 8 illustrates an alternative form of helical guide 40. The guide 40 is formed as an integral, rigid unit 70 having a tubular core 72 from which projects a helical fin 74. The unit 70 can be slid on to the inner conduit 22 with an interference fit, or be welded in position.

Although the helical insert or helical wire constructions of guide 40 are presently preferred, other constructions are also envisaged. For example, referring to Fig. 3, the guide could be formed integrally as a helical fin 44 on the outer surface of the inner conduit 22. Alternatively, referring to Fig. 4, the guide could be formed integrally as a helical rib 46 on the inner surface of the outer conduit 24.

Generally, it is preferred that the guide is in intimate contact with at least one of the conduits, and more preferably, with the outer conduit in particular (to provide optimum thermal contact with the tip region to be cooled). If the integrally formed guides of Figs. 3 and 4 are used, then the probe tip would preferably be manufactured to quite tight tolerances, in order to ensure that there is no (or only a very small) gap between the guide 44 or 46, and the confronting surface of the opposite conduit. Any gap might tend

to reduce the effectiveness of the guide, since cryogenic liquid may be able to leak around the guide, and take a more direct (less tortuous) path to the probe tip.

In the above arrangements, the probe is of a type in which the outer passage 28 is for the cryogen inlet, and the inner passage 26 is for the cryogen exhaust. In an alternative arrangement illustrated in Fig. 5, the roles of the inner passage 26 and the outer passage 28 are reversed. In Fig. 5, the same reference numerals are used where appropriate, and the numerals are suffixed to denote modifications, as explained below.

The transfer chamber 30' is modified to receive the inner conduit 22. The construction of the transfer chamber 30' is very similar to that described in the abovementioned GB patent publications. The exhaust port 20' communicates directly with the outer passage 28.

The guide 40 remains in the space between the inner conduit 22 and the outer conduit 24, such that the guide is now at the entry to the exhaust path. Nevertheless, the guide still functions in the same way as described above, to pro-long the time in which the cryogen is at, or adjacent to, the tip region and to increase the thermal coupling between the cryogenic fluid and the tip region of the probe.

The above embodiments employ a helical guide for defining a helical flow path for the cryogen. It will be appreciated that, in other embodiments, alternative tortuous flow paths may be used instead. For example, Fig. 9 illustrates an arrangement of baffles 50 and 52 to provide a tortuous path in place of the guide 40. Alternate baffles 50 and 52 project from the upper and lower surfaces, respectively, of the inner conduit 24 to define a sinusoidal-type path. Other tortuous path arrangements may be used as desired.

Although the embodiments illustrated use a single tortuous channel (for example, only one path through the helical shape), it will be appreciated that other embodiments may employ two or more channels (in parallel) as desired. For example, a multi-start helix shape may be used having multiple paths in a manner similar to a multi-start screw thread.

It will be appreciated that the invention, particularly as described in the preferred embodiments, can provide excellent thermal coupling at the cooling region, with the cryogenic fluid.

It will be appreciated that the above description is merely illustrative of preferred embodiments of the invention, and that many modifications may be made within the scope and/or principles of the invention. Although features believed to be of importance have been identified in the appended claims, the Applicant claims protection for any novel feature or idea described herein and/or illustrated in the drawings, whether or not emphasis has been placed thereon.

CLAIMS

1. Cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of cryogen liquid, the apparatus comprising means located at, or adjacent to, the cooling region for defining a tortuous flow path for cryogen fluid through, or around said means.

2. Apparatus according to claim 1, wherein the tortuous path is predetermined or is predeterminable.

3. Apparatus according to claim 1 or 2, wherein there are a number of tortuous paths, said number being not greater than about 20.

4. Apparatus according to claim 1, 2 or 3, wherein said means is in intimate contact with an external wall portion of the apparatus at, or adjacent to, the cooling region.

5. Apparatus according to claim 1, 2, 3 or 4, wherein said means is located at the point of entry of a cryogen inlet passage to a liquid vaporization region of said apparatus.

6. Apparatus according to claim 1, 2, 3 or 4 wherein said means is located at the entry of a cryogenic fluid exhaust path leading from a liquid vaporization region of said apparatus.

7. Apparatus according to any preceding claim, wherein said means defining the tortuous path is made at least partly of heat conductive material.

8. Apparatus according to any preceding claim, wherein the tortuous path is generally helical.

9. Cryosurgical apparatus comprising a cooling region which, in use, is cooled by vaporization of liquid cryogen, and means located at, or adjacent to, the cooling region and defining a generally helical cryogen flow path.

10. Apparatus according to claim 8 or 9, wherein the means defining the helical path comprises a strip or fin having a helical configuration around a central carrier.

11. Apparatus according to claim 10, wherein the central carrier is a first of a plurality of conduits, the strip or fin being received between two concentric conduits to define a helical path therebetween.

12. Apparatus according to claim 10 or 11, wherein the strip is a wire.

13. Apparatus according to any preceding claim , wherein, in use, the tortuous path results in the creation of a non-circular iceball shape.

14. Apparatus according to claim 13, wherein the iceball does not extend beyond a predetermined extremity of the apparatus.

15. Apparatus according to claim 13 or 14, wherein the iceball shape includes a region which is concave or generally non-convex.

16. Apparatus according to claim 13, 14 or 15, wherein the iceball shape includes a waist.

17. Apparatus according to any preceding claim, wherein the apparatus comprises a cryosurgical probe, and the cooling region is located on the probe.

18. Apparatus according to claim 17, wherein the cooling region is located at, or adjacent to, the tip of the probe.

19. A cryosurgical probe comprising a probe tip, a boiling region at or adjacent to the probe tip for generating cooling by vaporization of liquid cryogen supplied through the tip, and means located at or adjacent to the tip for defining a non-axial flow path, the flow path having a path length greater than the axial length of said means.

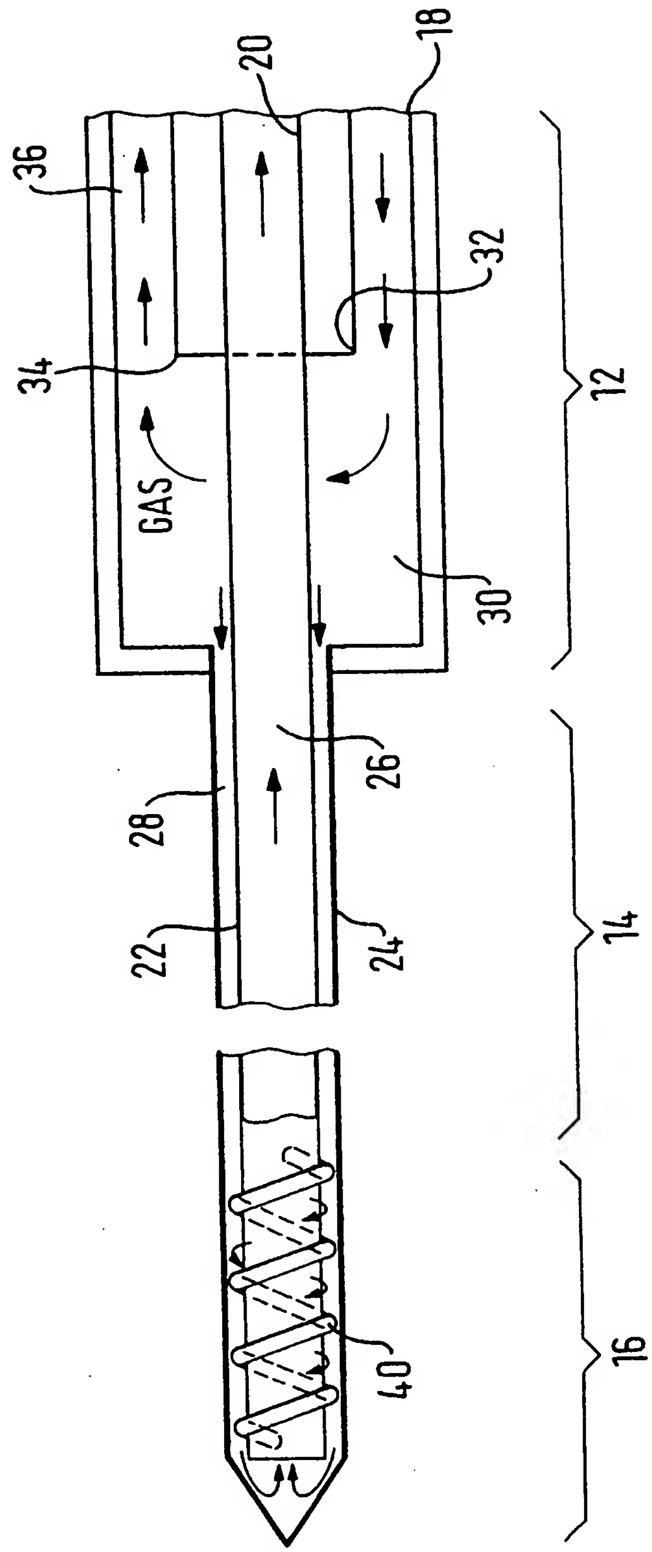


FIG. 1

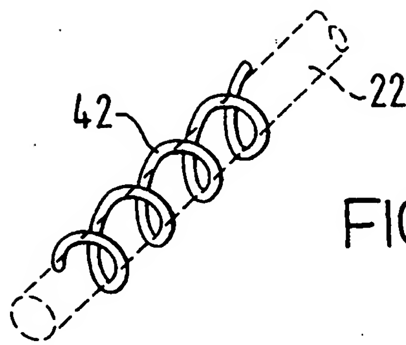


FIG. 2

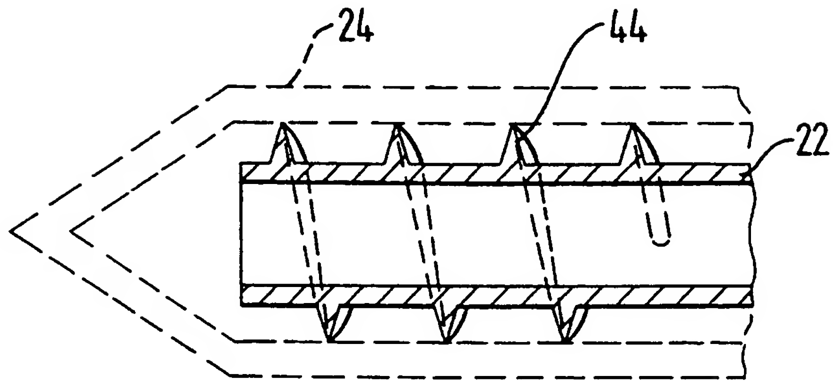


FIG. 3

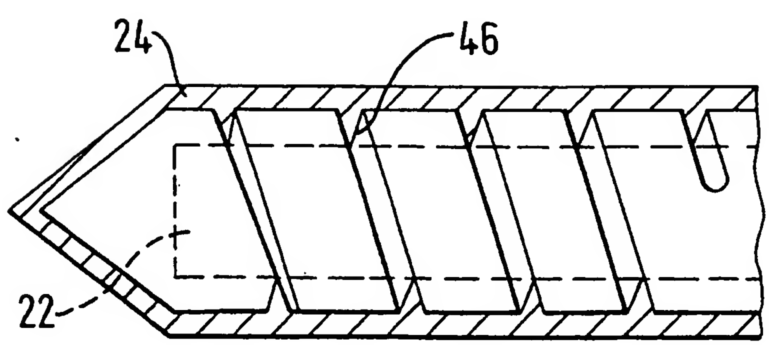


FIG. 4

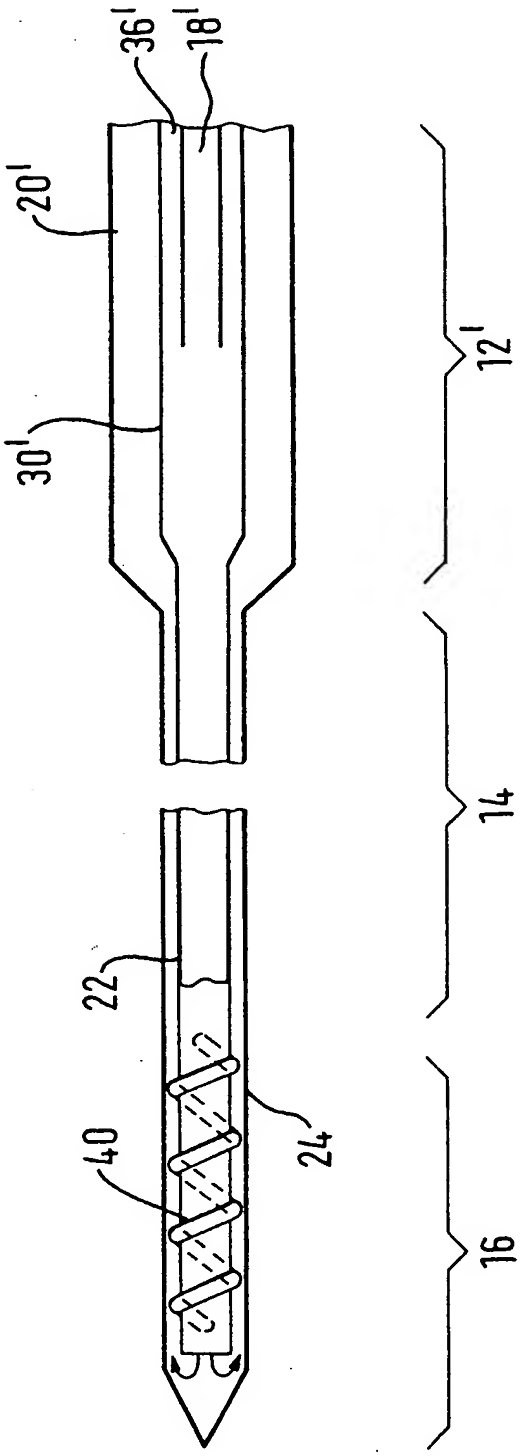


FIG. 5

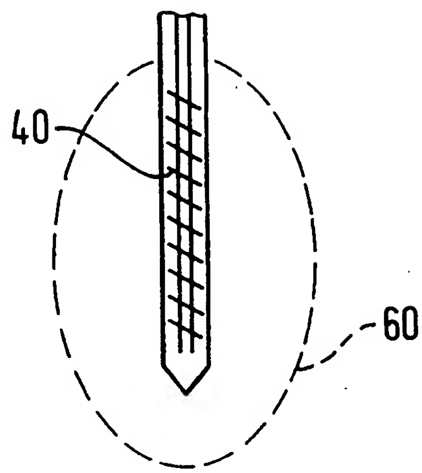


FIG. 6a

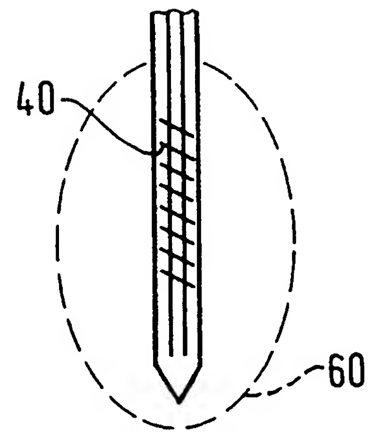


FIG. 6b

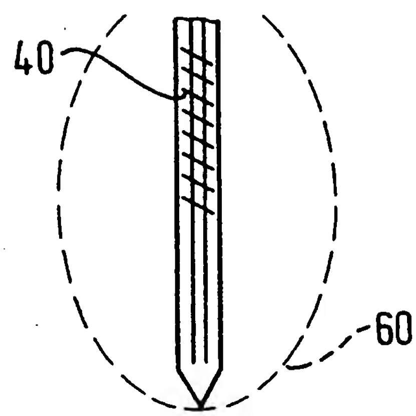


FIG. 6c

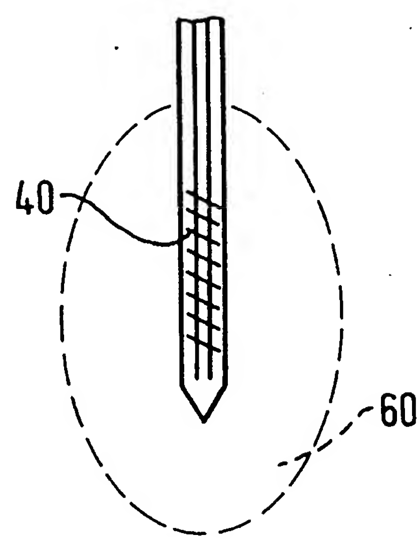


FIG. 6d

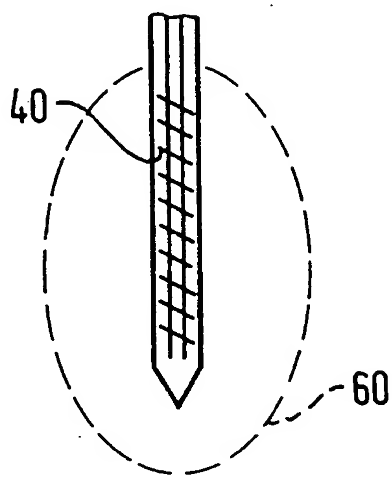


FIG.7a

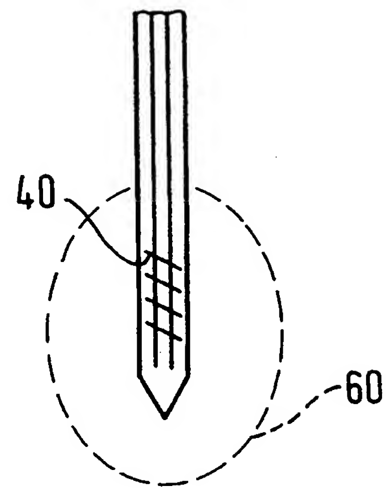


FIG.7b

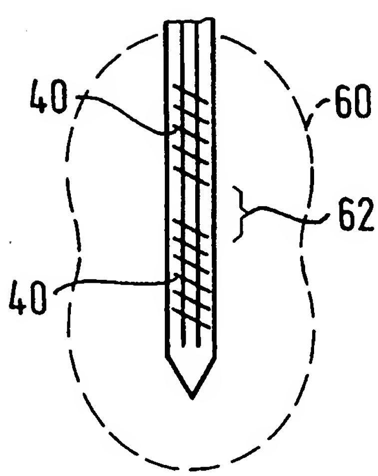


FIG.7c

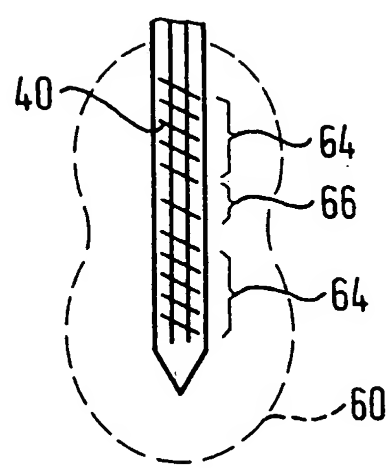


FIG.7d

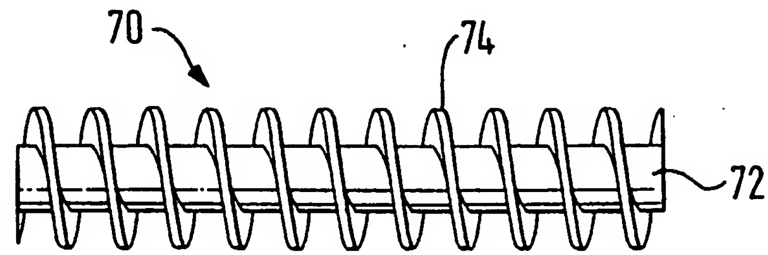


FIG. 8

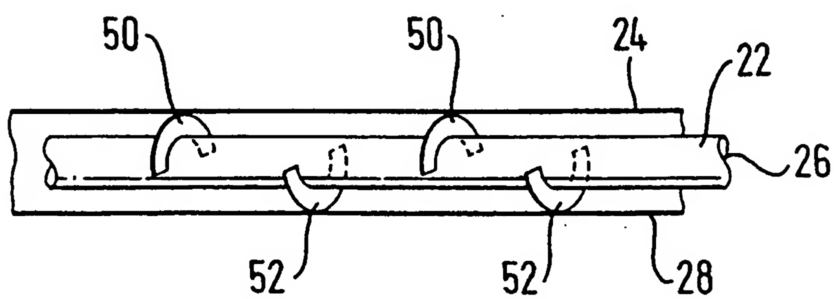


FIG. 9

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 99/01354

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B17/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 04221 A (ENDOCARE INC) 5 February 1998 (1998-02-05)	1-5,7-11
X	page 8, line 36 - page 9, line 15	13-19
Y	figure 3 page 10, line 36 - page 11, line 5; figure 3	6
X	GB 2 283 678 A (SPEMBLY MEDICAL LTD) 17 May 1995 (1995-05-17) page 6, line 36 - page 7, line 9; figure 3	1-4,7-11
X	EP 0 395 307 A (CRYO INSTR INC) 31 October 1990 (1990-10-31)	1-4,6,7, 19
A	column 5, line 33 - column 6, line 3; figure 3	10-12

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 July 1999	28/07/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mayer, E

1

INTERNATIONAL SEARCH REPORT

In ational Application No
PCT/GB 99/01354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 93 20769 A (IMPLEMED INC) 28 October 1993 (1993-10-28) page 7, line 6 - line 13; figures 1,4	6

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 99/01354

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9804221 A	05-02-1998	US 5800487 A	01-09-1998
		US 5800488 A	01-09-1998
		AU 3806597 A	20-02-1998
		EP 0925045 A	30-06-1999
GB 2283678 A	17-05-1995	DE 69416685 D	01-04-1999
		EP 0726734 A	21-08-1996
		EP 0857464 A	12-08-1998
		WO 9513025 A	18-05-1995
		JP 9506272 T	24-06-1997
EP 0395307 A	31-10-1990	US 4946460 A	07-08-1990
		AU 620508 B	20-02-1992
		AU 5380190 A	01-11-1990
		CA 2015104 A	26-10-1990
		JP 2299647 A	11-12-1990
		WO 9012546 A	01-11-1990
WO 9320769 A	28-10-1993	US 5281213 A	25-01-1994
		US 5281215 A	25-01-1994
		CA 2118011 A	28-10-1993
		EP 0680284 A	08-11-1995
		JP 7508666 T	28-09-1995
		US 5423807 A	13-06-1994